REMARKS

The Ex Parte Quayle Office Action mailed on April 14, 2008 and the comments therein have been carefully considered. Applicants appreciate the Examiner's consideration of Applicants' prior remarks and acknowledgement of allowable subject matter.

I. Status of Claims

Withdrawn Claims 1 - 7, drawn to an invention nonelected with traverse in the reply filed on 14 February 2002 have been canceled. Applicants have herein amended dependent claim 24 to include saliva as a biological sample. Independent claim 18, from which 24 depends, includes a biological sample for the assay. Support for such an amendment may be found, for example, in the specification on page 33, line 1. In addition, Applicants have added new dependent claim 32, support for which may be found in, for example, the specification in Example V, page 47, line 19. The undersigned telephonically discussed the claim amendments with Primary Examiner Elizabeth Kemmerer on June 13, 2008.

II. New Objection under 35 U.S.C. §132(a)

The Examiner has objected to the substitute sequence listing as new matter under 35 U.S.C. §132(a) and cites Ex Parte Maizel 27 USPQ2d 1662 (1992) as guidance as to how to correct sequence errors. In general, the Board of Patent Appeals and Interferences in the Maizel case states that "the question of whether or not a change in the chemical structure of a DNA sequence set forth in the specification is permitted depends on the facts of each case and the significance of the modification..." *Id* at 1666. As explained in detail below, Applicants submit that the substitute sequence listing is not significant in nature and does not modify the claims or the specification.

In SEQ ID NO: 1 and SEQ ID NOs: 3-6, there is a one amino acid difference between the sequence as listed in the GenBank report and the sequence listing in the patent application located at position 540 (i.e. Lys should be Asn). *See* the GenBank report attached hereto as Appendix B. This is a conservative amino acid change that is not predicted to affect the function or structure of the proteins. *See* Ex Parte Maizel 27 USPQ2d 1662 at 1666 (recognizing "that single amino acid substitutions *usually* do not significantly alter the biological activity of proteins"). *See* also ¶17 in the Declaration of Nita. J. Maihle attached hereto as Appendix A. It is also the site of a reported HindIII polymorphism, which encodes either Asn or Lys. *See* the Declaration of Nita J. Maihle attached hereto as Appendix A. The more correct sequence was submitted to GenBank on February 1, 1999, which is about 7 months prior to the priority date for the instant application, which is September 30, 1999, thus indicating that Applicants were in possession of the sequences at the time of filing. *See* the Declaration of Nita J. Maihle attached hereto as Appendix A and the GenBank report attached hereto as Appendix B. Furthermore, the description of the sequences and proteins (both structure and function) in the specification, such as found in Examples I-III, is correct as filed, i.e. this is merely a discrepancy in the sequence listing itself that should be corrected for accuracy. *See* the Declaration of Nita. J. Maihle attached hereto as Appendix A

In SEQ ID NO: 2, there are five independent discrepancies between the sequence listing of the application and the sequence submitted to GenBank, also submitted February 1, 1999: 1) at position 706, 'a' should be 'c'; 2) at position 1865 'g' should be 'c'; 3) at position 2394 'a' should be 'g'; 4) positions 2435-2437 should be three 'c's instead of two; and 5) at position 2589 'g' should be 't'. *See* Appendix B. Applicants were in possession of both the nucleotide and polypeptide sequences at the time of filing. *See* ¶18 in the Declaration of Nita J. Maihle attached

hereto as Appendix A. SEQ ID NO: 2 corresponds with the protein sequence of SEQ ID NO: 1. Position 1865 corresponds with the HindIII polymorphism, described above, associated with the amino acid at position 540. *See* the Declaration of Nita J. Maihle attached hereto as Appendix A. Further, unpublished preliminary data from the time of submitting these sequences suggests that positions 2394 and 2589 are likely sites of naturally occurring sequence polymorphisms (a/g at 2394 and g/t at 2589). See the Declaration of Nita. J. Maihle attached hereto as Appendix A. Because polymorphisms are naturally occurring, they are similar to the "inherent characteristics" supported in the case of Ex Parte Marsili. *See* 214 USPQ 904 (1979). The coding sequence of SEQ ID NO: 2 is 246-2363. *See* GenBank report attached hereto as Appendix B. Positions 2394, 2435, and 2589 are all in the 3'-UTR region outside of the coding region, thus they would not alter the structure of the translated protein product. *See* Declaration of Nita J. Maihle attached as Appendix A. These discrepancies, including position 706, are likely typographical errors in the sequence listing of the '380 Application, as further evidenced by the fact that the nucleotide sequence, SEQ ID NO: 2, has independent discrepancies from SEQ ID NO:1. No matter how the errors resulted, the nature of the errors is not significant in that they do not affect the structure or function of the proteins. *See* the Declaration of Nita J. Maihle attached hereto as Appendix A. The description of the nucleotide sequence as found in the specification, such as Example I, is correct, including the description, isolation, primers, etc.

Applicants submit that one skilled in the art would readily associate the sequence listing as filed with the correct GenBank listing as reflected in the GenBank report attached hereto as Appendix B and further correlate the listings with soluble EGFR/sErbB1 as described in the application as well as subsequent publications based on not only the sequence listings alone but also the description in the specification as filed, which is correct. *See* ¶¶19-20 in the Declaration

of Nita J. Maihle, Appendix A. *See also* Ex Parte Maizel 27 USPQ2d 1662 at 1667 (stating the issue as "whether the description of the claimed compound in the original disclosure is adequate to identify and distinguish the claimed subject matter".) Furthermore, the sequence amendments for this application are distinguishable from those in Maizel, which were not adequately described to indicate possession. *Id* at 1667. *See* also Ex Parte Marsili 214 USPQ 904 (1979) and Fiers v. Revel 25 USPQ2d 1601, 1605 (both indicating, similar to Ex Parte Maizel, the significance of the description to adequately distinguish and prove possession). The amendments in Ex Parte Marsili were allowed, with the issue being "the question of *changing* the original description of a product which is admittedly patentable and was described by sufficient characteristics to distinguish it…[not]… the question of *adding* characteristics not previously mentioned." *See* 214 USPQ 904 (1979).

Applicants were in possession of the sequences at the time of filing as indicated by the prior submissions to GenBank. In addition, a clear and accurate description of the sequences can be found in the specification as filed, i.e. no new matter, and the discrepancies between the sequence listing and the "correct" GenBank listing are insignificant in nature. Applicants respectfully request the sequence listing be amended for accuracy.

III. Conclusion

Applicants have fully responded to the Ex Parte Quayle action by canceling the nonelected claims and by describing the nature of the amendments made in the previously filed substitute sequence listing. Accordingly, Applicants respectfully request reconsideration of the objection and a notice of allowance.

The Commissioner is hereby authorized to charge Deposit Account No. 03-2026 for any fees associated with this amendment or credit any overpayments.

Applicants would appreciate a telephone call to the undersigned attorney of record should the Examiner have any questions or comments with respect to this response for purposes of efficiently resolving same.

Respectfully submitted,

By 

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